

**AMENDMENTS TO THE CLAIMS**

1. (Previously presented): A pharmaceutical agent delivery composition comprising:

(a) a transport polymer comprising a peptide, characterized as having at least 10 amino acid residues, and wherein at least 10% of said amino acid residues are histidine, and wherein at least 10% of said amino acid residues are selected from the group consisting of non-histidine amino acids with a side-group that carries a positive charge at physiological pH, and wherein the molecular structure of said peptide is selected from the group consisting of:

linear, with the proviso that said peptide does not comprise a hexa-peptide having the sequence His-His-His-His-His-His, unless at least 10% of the remaining amino acid residues of said peptide are histidine; and

branched, with a backbone peptide of 1 or more amino acid residues and at least one peptide branch of 1 or more amino acid residues covalently attached to a side-group of an amino acid residue of said backbone peptide, with the proviso that each peptide branch can consist of a single histidine residue only if the backbone peptide does not consist solely of lysine residues;

with the proviso that said transport polymer does not consist of:

a random histidine copolymer; or

a block copolymer of histidine and a non-histidine amino acid with a side-group that carries a positive charge at physiological pH;

(b) a pharmaceutical agent associated with said transport polymer; and

(c) optionally, at least one intracellular delivery component associated with said transport polymer and/or said pharmaceutical agent.

2. (Previously presented): The pharmaceutical agent delivery composition of claim 1, wherein at least 20% of the amino acid residues of said peptide are histidine, and wherein at least 20% of said amino acid residues are selected from the group consisting of non-histidine amino acids with a side-group that carries a positive charge at physiological pH.

3. (Previously presented): The pharmaceutical agent delivery composition of claim 2, wherein said peptide comprises a subsegment of amino acid residues selected from the group consisting of:

K-H-K-H-K-H-K-H-K-H (SEQ ID NO: 14),

K-H-K-H-K-H-K-G-K-H-K-H-K (SEQ ID NO:1),

K-H-K-H-K-H-K-G-K-H-K-H-K-H-K (SEQ ID NO:2),

K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:3),

K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:4),

K-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-K (SEQ ID NO:5),

K-K-H-H-H-K-H-H-H-K-K-H-H-H-K-H-H-H-K-K (SEQ ID NO:6),

H-H-K-H-H-K-H-H-K-H-H-K-H-H-K (SEQ ID NO:15),

K-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-K (SEQ ID NO:16),

end-to-end repeats of one or more of the above sequences, and

the reverse of any of the above sequences.

4. (Previously presented): The pharmaceutical agent delivery composition of claim 2, further comprising at least one intracellular delivery component associated with said transport polymer and/or said pharmaceutical agent.

5. (Original claim): The pharmaceutical agent delivery composition of claim 4, wherein said intracellular delivery component comprises a lipid.

6. (Previously presented): The pharmaceutical agent delivery composition of claim 2, further comprising a transition metal.

7. (Previously presented): The pharmaceutical agent delivery composition of claim 2, wherein said pharmaceutical agent consists of at least one therapeutic agent.

8. (Original): The pharmaceutical agent delivery composition of claim 7, wherein said therapeutic agent is selected from the group consisting of a protein, an oligopeptide, a nucleic acid, a cancer chemotherapeutic agent, an infectious disease chemotherapeutic agent, and any combination of two or more of the above.

9. (Original): The pharmaceutical agent delivery composition of claim 8, wherein said therapeutic agent is nucleic acid.

10. (Original): The pharmaceutical agent delivery composition of claim 9, wherein said nucleic acid is an antisense oligonucleotide, a ribozyme, an RNA-cleaving DNA oligonucleotide, or a combination of two or more of the above.

11. (Cancelled).

12. (Original): A method for delivering a pharmaceutical agent to the interior of a cell, said method comprising a step of contacting the cell with the pharmaceutical agent delivery composition of claim 1.

13. (Previously presented): The method of claim 22, wherein the molecular structure of said peptide is branched.

14. (Previously presented): The method of claim 22, wherein said peptide comprises a subsegment of amino acid residues selected from the group consisting of:

K-H-K-H-K-H-K-H-K-H (SEQ ID NO: 14),

K-H-K-H-K-H-K-G-K-H-K-H-K (SEQ ID NO:1),

K-H-K-H-K-H-K-G-K-H-K-H-K-H-K (SEQ ID NO:2),

K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:3),

K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:4),

K-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-K (SEQ ID NO:5),

K-K-H-H-H-K-H-H-H-K-K-H-H-H-K-H-H-H-K-K (SEQ ID NO:6),

H-H-K-H-H-K-H-H-K-H-H-K-H-H-K (SEQ ID NO:15),

K-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-K (SEQ ID NO:16),

end-to-end repeats of one or more of the above sequences, and

the reverse of any of the above sequences.

15. (Previously presented): The method of claim 22, wherein said pharmaceutical agent delivery composition further comprises at least one intracellular delivery component associated with said transport polymer and/or said pharmaceutical agent.

16. (Original): The method of claim 15, wherein said intracellular delivery component comprises a lipid.

17. (Previously presented): The method of claim 22, wherein said pharmaceutical agent delivery composition further comprises a transition metal.

18. (Previously presented): The method of claim 22, wherein said pharmaceutical agent consists of at least one therapeutic agent.

19. (Original): The method of claim 18, wherein said therapeutic agent is selected from the group consisting of a protein, an oligopeptide, a nucleic acid, a cancer chemotherapeutic agent, an infectious disease chemotherapeutic agent, and any combination of two or more of the above.

20. (Original): The method of claim 19, wherein said therapeutic agent is nucleic acid.

21. (Original): The method of claim 20, wherein said nucleic acid is an antisense oligonucleotide, a ribozyme, an RNA-cleaving DNA oligonucleotide, or a combination of two or more of the above.

22. (Previously presented): The method of claim 12, wherein at least 20% of the amino acids of said peptide are histidine and at least 20% of the non-histidine amino acid residues of said peptide carry a positive charge at physiological pH.

23. (Previously presented): The method of claim 22, further comprising the steps of:

removing said cell from a subject prior to contacting said cell with said pharmaceutical agent

delivery composition; and

administering said cell to said subject after contacting said cell with said pharmaceutical agent

delivery composition.

24. (Original): The method of claim 23, wherein said pharmaceutical agent delivery composition further comprises an intracellular delivery component.

25. (Previously presented): A method for producing a pharmaceutical agent delivery composition comprising the steps of:

- a. providing a transport polymer comprising a peptide characterized as having at least 10 amino acid residues, and wherein at least 10% of said amino acid residues are histidine, and wherein at least 10% of said amino acid residues are selected from the group consisting of non-histidine amino acids with a side-group that carries a positive charge at physiological pH, and wherein the molecular structure of said peptide is selected from the group consisting of:
  - linear, with the proviso that said peptide does not comprise a sequence His-His-His-His-His-His, unless at least 10% of the remaining amino acid residues of said peptide are histidine; and
  - branched, with a backbone peptide of 1 or more amino acid residues and at least one peptide branch of 1 or more amino acid residues covalently attached to a side-group of an amino acid residue of said backbone peptide, with the proviso that each peptide branch can consist of a single histidine residue only if the backbone peptide does not consist solely of lysine residues;with the proviso that said transport polymer does not consist of:
  - a random histidine copolymer; or
  - a block copolymer of histidine and a non-histidine amino acid with a side-group that carries a positive charge at physiological pH;
- b. providing a pharmaceutical agent capable of associating with said transport polymer;
- c. combining said transport polymer with said pharmaceutical agent to form a polymer/pharmaceutical agent complex; and
- d. mixing said complex with an intracellular delivery component.

26. (Original): The method of claim 25, wherein said intracellular delivery component comprises a lipid.

27. (Previously presented): A pharmaceutical agent delivery composition comprising:

- (a) a pharmaceutical agent;

(b) a transport polymer in association with the pharmaceutical agent, the transport polymer comprising a peptide characterized as having at least 10% of the amino acid residues are histidine and at least 10% of the amino acid residues are non-histidine, wherein the non-histidine residues are selected so as to tailor the transport polymer to the pharmaceutical agent and a method of association between the pharmaceutical agent and the transport polymer, and wherein the molecular structure of the peptide is selected from the group consisting of:

linear and having at least 13 amino acids, with the proviso that:

- a. the entire sequence of said peptide cannot be described by the formula:  $(XHHX)_n$ , wherein H is histidine, X is a hydrophobic amino acid, and n is an integer greater than or equal to 4;
- b. the entire sequence of said peptide cannot be described by the formula:  $(XHHX)_n$ , wherein H is histidine, X is a hydrophobic amino acid, and n is an integer greater than or equal to 4; and
- c. said peptide does not comprise a hexa-peptide having the sequence His-His-His-His-His-His, unless at least 10% of the remaining amino acid residues of said peptide are histidine; and

branched and having at least 40 amino acids, with a backbone of 1 or more amino acid residues and at least one branch of 1 or more amino acid residues covalently attached to a side-group of an amino acid residue of said backbone, with the proviso that each branch can consist of a single histidine residue only if the backbone does not consist solely of lysine residues;

with the proviso that said transport polymer does not consist of:

- a random histidine copolymer; or
- a block copolymer of histidine and a non-histidine amino acid with a side-group that carries a positive charge at physiological pH; and

(c) optionally, at least one intracellular delivery component associated with said transport polymer and/or said pharmaceutical agent.

28. (Previously presented): The pharmaceutical agent delivery composition of claim 27, wherein the pharmaceutical agent has an overall net negative charge, wherein at least 20% of the amino acid residues of said peptide are histidine, and wherein at least 20% of said amino acid residues are selected from the group consisting of non-histidine amino acids with a side-group that carries a positive charge at physiological pH.

29. (Currently amended): The pharmaceutical agent delivery composition of claim 28, wherein the pharmaceutical agent comprises nucleic acid and wherein ~~at least about 40% of said amino acid residues of said peptide are selected from the group consisting of non-histidine residues which carry a positive charge at physiological pH and at least about 27%~~ **about 40% to about 60%** of said amino acid residues of said peptide are histidine.

30. (Previously presented): The pharmaceutical agent delivery composition of claim 29, wherein the non-histidine residues are each independently selected from the group consisting of lysine and glycine.

31. (Previously presented): The pharmaceutical agent delivery composition of claim 29, further comprising at least one intracellular delivery component.

32. (Previously presented): The pharmaceutical agent delivery composition of claim 31, wherein the intracellular delivery component comprises a lipid.

33. (Previously presented): The pharmaceutical agent delivery composition of claim 32, wherein the lipid is a cationic lipid.

34. (Previously presented): The pharmaceutical agent delivery composition of claim 32, wherein the molecular structure of the peptide is linear.

35. (Previously presented): The pharmaceutical agent delivery composition of claim 29, wherein the molecular structure of the peptide is branched.

36. (Previously presented): The pharmaceutical agent delivery composition of claim 28, wherein the pharmaceutical agent comprises a therapeutic agent selected from the group consisting of an antisense oligonucleotide, a ribozyme, an RNA-cleaving DNA oligonucleotide, an expression vector, and a combination of two or more of the above.

37. (Previously presented): The pharmaceutical agent delivery composition of claim 36, wherein the therapeutic agent is an RNA-cleaving DNA oligonucleotide which targets VEGF receptor mRNA.

38. (Previously presented): The pharmaceutical agent delivery composition of claim 28, wherein said peptide comprises a segment of amino acid residues selected from the group consisting of:

K-H-K-H-K-H-K-H-K-H (SEQ ID NO: 14),

K-H-K-H-K-H-K-G-K-H-K-H-K (SEQ ID NO:1),

K-H-K-H-K-H-K-G-K-H-K-H-K-H-K (SEQ ID NO:2),

K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:3),

K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:4),

K-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-K (SEQ ID NO:5),

K-K-H-H-H-K-H-H-H-K-K-H-H-H-K-H-H-H-K-K (SEQ ID NO:6),

H-H-K-H-H-K-H-H-K-H-H-K-H-H-K (SEQ ID NO:15),

K-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-K (SEQ ID NO:16),

end-to-end repeats of one or more of the above sequences, and the reverse of any of the above sequences.

39. (Previously presented): The pharmaceutical agent delivery composition of claim 27, further comprising a transition metal.

40. (Previously presented): A method for delivering a pharmaceutical agent to the interior of a cell, said method comprising a step of contacting the cell with the pharmaceutical agent delivery composition of claim 27.



41. (Previously presented): The method of claim 40, wherein the pharmaceutical agent has an overall net negative charge, wherein at least 20% of the amino acid residues of said peptide are histidine, and wherein at least 20% of said amino acid residues are selected from the group consisting of non-histidine amino acids with a side-group that carries a positive charge at physiological pH.

42. (Currently amended): The method of claim 41, wherein the pharmaceutical agent comprises nucleic acid and wherein ~~at least about 40% of said amino acid residues of said peptide are selected from the group consisting of non-histidine residues which carry a positive charge at physiological pH and at least about 27%~~ **about 40% to about 60%** of said amino acid residues of said peptide are histidine.

43. (Previously presented): The method of claim 42, wherein the non-histidine residues are each independently selected from the group consisting of lysine and glycine.

44. (Previously presented): The method of claim 41, wherein the pharmaceutical agent delivery composition further comprises at least one intracellular delivery component, wherein the intracellular delivery component comprises a cationic lipid.

45. (Currently amended): The pharmaceutical agent delivery composition of claim 2, wherein ~~at least about 27%~~ **about 40% to about 60%** of the amino acid residues of said peptide are histidine.

46. (Currently amended): The pharmaceutical agent delivery composition of claim 9, wherein ~~at least about 27%~~ **at least about 40%** of the amino acid residues of said peptide are histidine.

47. (Previously presented): The pharmaceutical agent delivery composition of claim 46, wherein said pharmaceutical agent delivery composition further comprises an intracellular delivery component.

48. (Currently amended): The pharmaceutical agent delivery composition of claim 47, wherein ~~at least about 40% of said amino acid residues are selected from the group consisting of non-histidine amino acids with a side-group that carries a positive charge at physiological pH~~ **about 40% to about 60% of the amino acid residues of said peptide are histidine.**

49. (Currently amended): The method of claim 22, wherein ~~at least about 27%~~ **about 40% to about 60%** of the amino acids of said peptide are histidine.

50. (Currently amended): The pharmaceutical agent delivery composition of claim 28, wherein ~~at least about 27%~~ **about 40% to about 60%** of the amino acids of said peptide are histidine.

51. (Currently amended): The method of claim 41, wherein ~~at least about 27%~~ **about 40% to about 60%** of the amino acids of said peptide are histidine.

52. (Previously presented): The pharmaceutical agent delivery composition of claim 29, wherein said peptide is selected from the group consisting of linear and having less than about 50 amino acids, and branched and having less than about 300 amino acids.